AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

In the claims

Claim 1 (original): Use of a multifunctional steroid compound comprising

i) a steroid component,

ii) at least one SOD mimic component, and optionally

iii) at least one NO donor component

in the preparation of a medicament.

Claim 2 (original): Use of a multifunctional steroid compound according to claim 1, comprising

i) a steroid component,

ii) at least one SOD mimic component linked to said steroid component, and

iii) at least one NO donor component linked to said steroid component.

Claim 3 (original): Use according to claim 1, wherein said steroid comprises cyclopenta[a]phenantrene, said SOD mimic component comprises an antioxidant reacting with superoxide, and said NO donor comprises a group capable of providing nitric oxide in a form selected from uncharged, free radical, and charged.

Claim 4 (original): Use according to claim 1, wherein said SOD mimic component comprises a substituted N-oxide free radical.

Claim 5 (original): Use according to claim 4, wherein the N-atom of said N-oxide is a member of 3 to 7 membered heterocyclic ring.

Claim 6 (original): Use according to claim 2, wherein said NO donor component comprises a group selected from —ONO_2, —ONO, —SNO, and —NONOate.

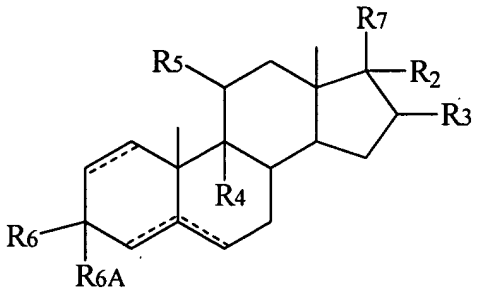
Claim 7 (currently amended): Use of a multifunctional steroid compound according to claim 1 ~~any one of claims 1 to 6~~ in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of disorders associated with oxidative stress and free radical injury, disorders in which treatment with steroids or their analogs is indicated, and disorders in which treatment with a smooth muscle relaxant is indicated.

Claim 8 (currently amended): Use of a multifunctional steroid compound according to claim 1 ~~any one of claims 1 to 6~~ in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of respiratory, pulmonary, cardiovascular, inflammatory, and autoimmune disorders.

Claim 9 (currently amended): Use of a multifunctional steroid compound according to claim 1 ~~any one of claims 1 to 6~~ in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, Chronic Obstructive Pulmonary Diseases (COPDs), bronchial hyperreactivity, respiratory distress syndrome or Chronic Obstructive Airway Disease (COADs), allergic conditions, arthritis, autoimmune hematologic disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-versus-host disease, multiple sclerosis, Alzheimer diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, disorders related to learning, disorders related to olfaction, disorders related to nociception, cerebral edema, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions,

drug and disease-induced neuropathies and nephropathies, pathological uterine contractions, sinus tachycardia, ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders, hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholestemia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion tissue injury, chemotaxis and phagocytic impairment in immunological disorders, aging–mediated changes, cerebrovascular diseases, thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection.

Claim 10 (currently amended): Use of a multifunctional steroid compound according to claim 1 ~~any one of claims 1 to 9~~, wherein said steroid compound has formula (4)



(4)

optical isomers thereof, salts thereof, and solvates thereof;

wherein ----- is a single or double bond, with the proviso that two double bonds are not adjacent;

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate,

—$OC(O)R^8$ wherein R^8 is C_1-C_5 alkyl or 5- or 6-member heteroaryl, or R^2 and R^7 together form a substituted N-oxide free radical;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

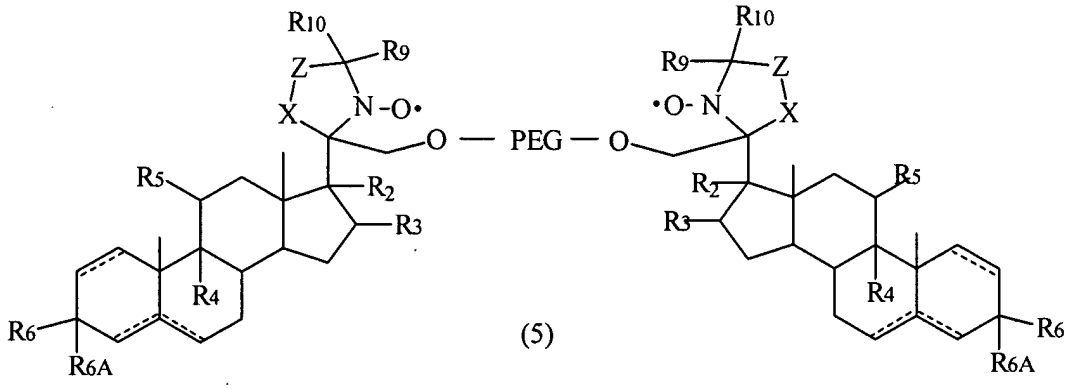
R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical;

R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate, and

R^{6A}, if present, is —H, or R^6 and R^{6A} together form a substituted N-oxide free radical;
R^7 is —H, —ONO, —ONO_2, —SNO, —NONOate, or a substituted N-oxide free radical wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring, which ring is optionally substituted by —$OCOCH_2$-PEG wherein said PEG may by optionally coupled to another steroid compound, and which ring is further optionally substituted by or one or more independently selected C_1-C_5 alkyl groups which may be further independently substituted by a group selected from an NO donor component, —SR^{11}, —halogen, and —$OC(O)R^{13}$ wherein R^{11} is C_1-C_5 alkyl and wherein R^{13} is C_1-C_5 alkyl or 5- or 6-member heteroaryl, or R^2 and R^7 together form a substituted N-oxide free radical; and
wherein NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate, and wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups which may be may be further independently substituted by an NO donor component.

Claim 11 (original): Use according to claim 10, wherein said steroid compound has formula (5)



(5)

wherein the R^2, R^3, R^4, R^5, R^6, and R^{6A} are as defined in claim 10;
R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the alkyl group is independently substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

and PEG is a polyethylene glycol of a molecular weight from about 100 to about 4000.

Claim 12 (original): Use according to claim 10, wherein said steroid compound has a formula selected from Ia to Id (below) wherein

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or

—OC(O)R^8, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

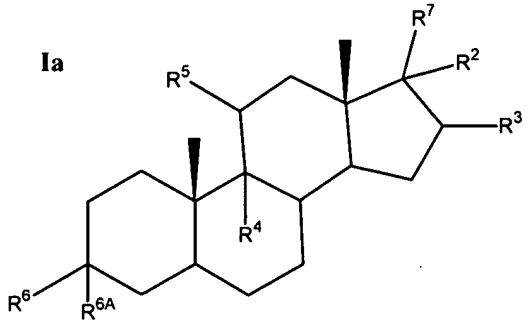
R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate, and

R^{6A}, if present, is —H, or R^6 and R^{6A} together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide

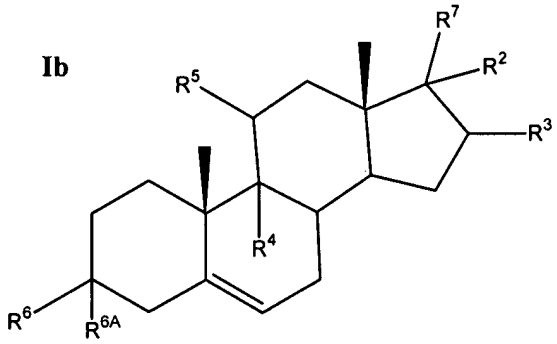
free radical is within a 5- or 6- member ring substituted by one or more independently selected C_1-C_5 alkyl groups which may be may be further independently substituted by an NO donor component;

R^7 is —H, —ONO, —ONO_2, —SNO, —NONOate, or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring optionally substituted by —$OCOCH_2$-PEG or one or more independently selected C_1-C_5 alkyl groups which may be further independently substituted by an NO donor component, —SR^{11}— halogen, or —OC(O)R^{13}, wherein R^{11} is C_1-C_5 alkyl, and wherein

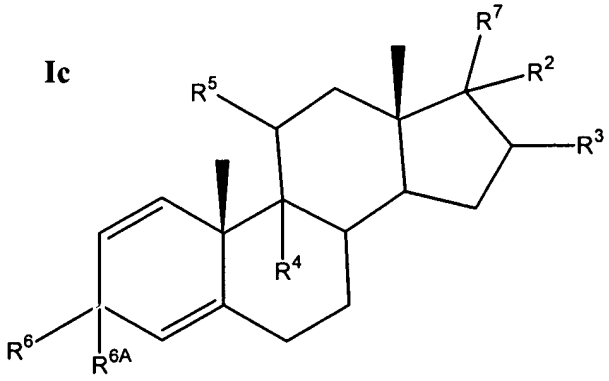
Ia


R7
R2
R5
R3
R4
R6
R6A

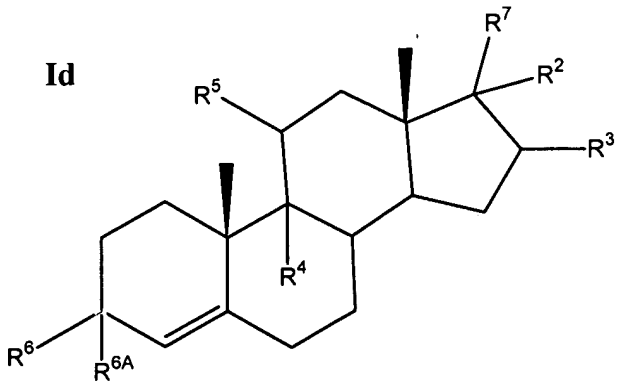
Ib


R7
R2
R5
R3
R4
R6
R6A

Ic


R7
R2
R5
R3
R4
R6
R6A

Id


R7
R2
R5
R3
R4
R6
R6A

R^{13} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl, or R^2 and R^7 together form a substituted N-oxide free radical; and

NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate;

wherein at least one of R^2, R^5, R^6, or R^7 comprises an NO donor; and

wherein at least one of R^5, R^6, or R^7 comprises a substituted N-oxide free radical.

Claim 13 (original): Use according to claim 10, wherein said steroid compound has a formula selected from IIa to IId (below) wherein

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or

—$OC(O)R^8$, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

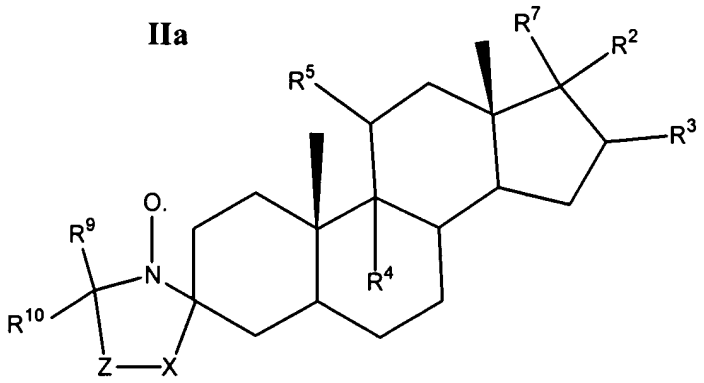
R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^7 is —H, —ONO, —ONO_2, —SNO, —NONOate, or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by

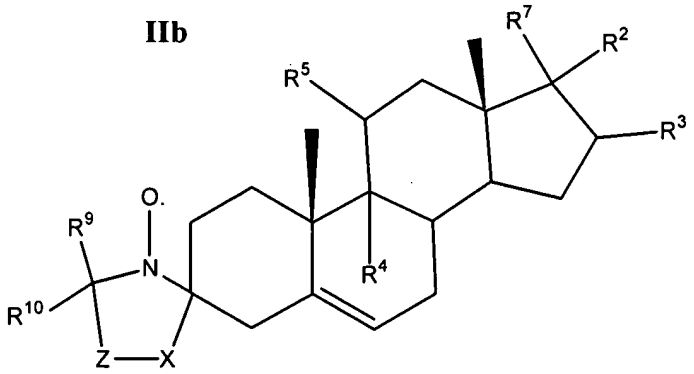
—$OCOCH_2$-PEG or by one or more independently selected C_1-C_5 alkyl groups, wherein said alkyl group may be further independently substituted by an NO donor, —SR^{11}, —halogen, or —$OC(O)R^{13}$, wherein R^{11} is C_1-C_5 alkyl, and wherein R^{13} is C_1-C_5 alkyl or 5- or 6-member heteroaryl;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups or substituted linear or branched C_1-C_5 alkyl groups wherein said alkyl group may be substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl or 5- or 6-member heteroaryl;

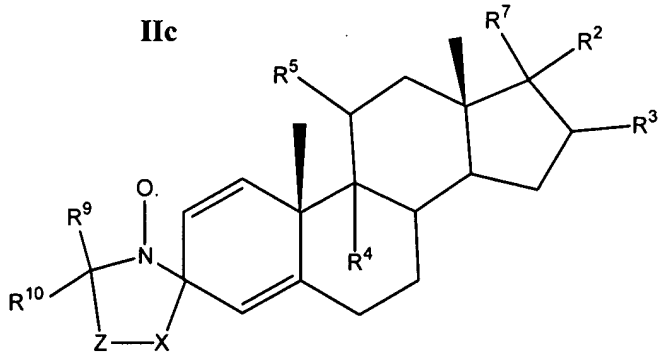
IIa



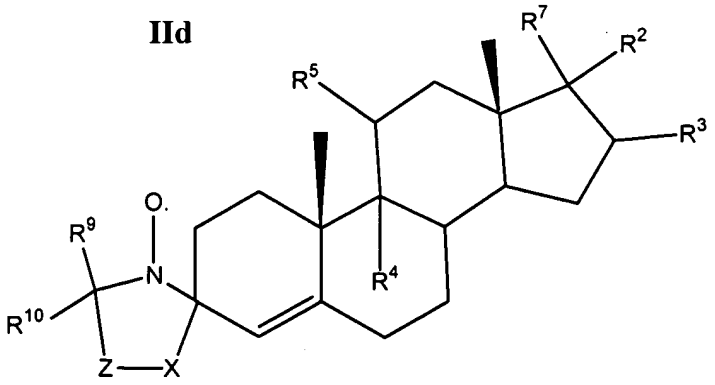
IIb



IIc



IId



X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^2, R^5, R^7, R^9 or R^{10} comprises an NO donor.

Claim 14 (original): Use according to claim 10, wherein said steroid compound has a formula selected from IIIa to IIId (below) wherein

R^1 is —H, —OH, —$OCOCH_2$-PEG, linear or branched C_1-C_5 alkyl, linear or branched C_1-C_5 alkyl substituted by an NO donor,—SR^{11}, —halogen, or —$OC(O)R^{15}$, wherein R^{11} is C_1-C_5 alkyl, wherein R^{15} is C_1-C_5 alkyl;

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or —$OC(O)R^8$, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

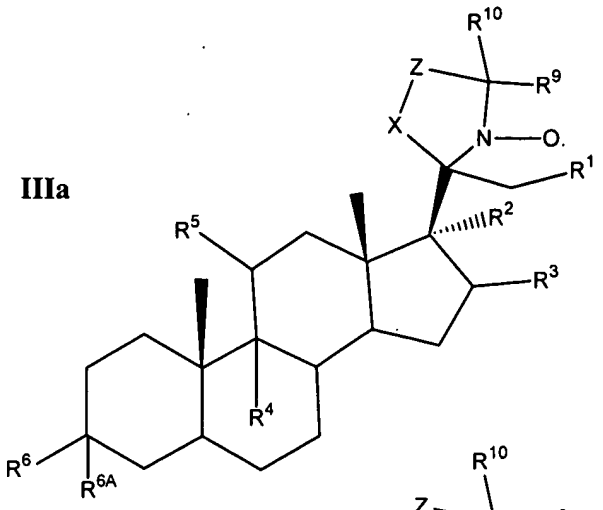
R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

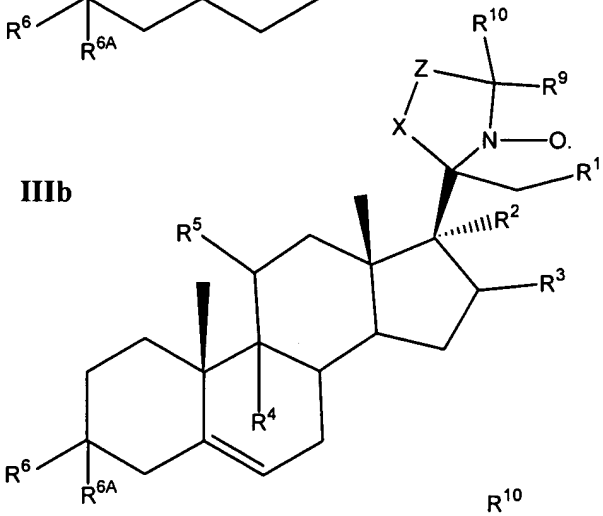
R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate, and R^{6A}, if present, is —H, or R^6 and R^{6A} together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C_1-C_5 alkyl groups, wherein said alkyl may be further substituted by an NO donor, or —$OC(O)R^{12}$, wherein R^{12} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein said alkyl group is

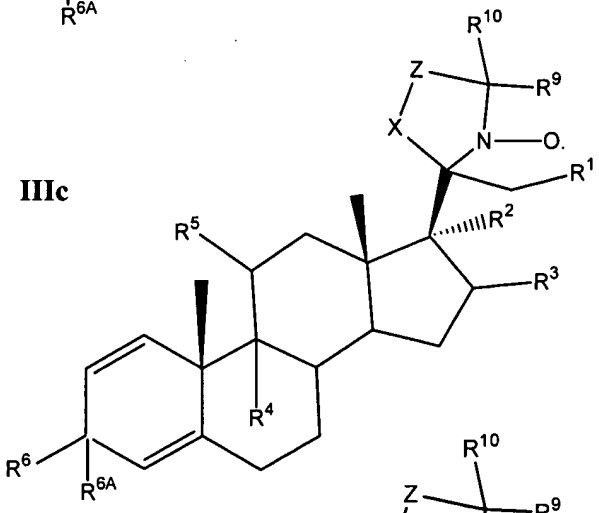
IIIa



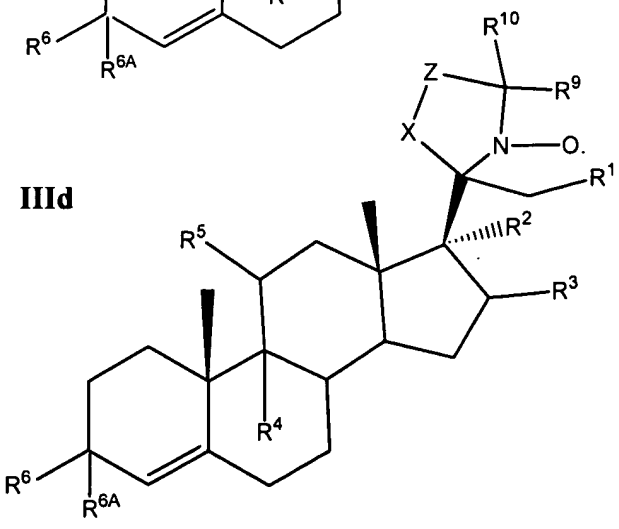
IIIb



IIIc



IIId



independently substituted by —ONO, —ONO_2, —SNO, —NONOate or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl;

X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^1, R^2, R^5, R^6, R^9 or R^{10} comprises at least one NO donor.

Claim 15 (original): Use according to claim 10, wherein said steroid compound has formula a formula selected from IVa to IVd (below) wherein

R^1 is —H, —OH, —$OCOCH_2$-PEG; linear or branched C_1-C_5 alkyl; linear or branched C_1-C_5 alkyl substituted by an NO donor, —SR^{11}, —halogen, or —$OC(O)R^{15}$, wherein R^{11} is C_1-C_5 alkyl, and wherein R^{15} is C_1-C_5 alkyl;

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or

—$OC(O)R^8$, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

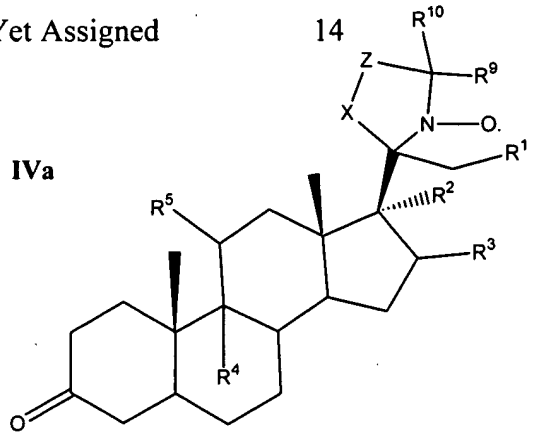
R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups; R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the said group is independently substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl;

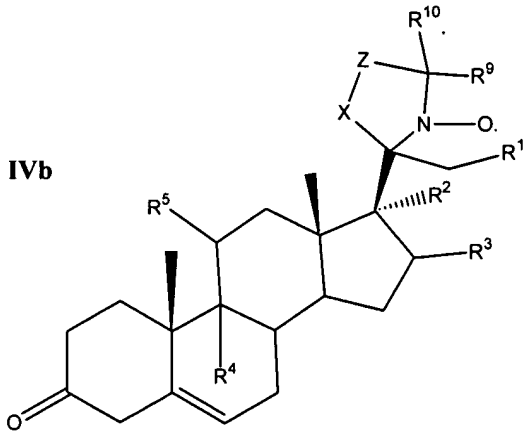
X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

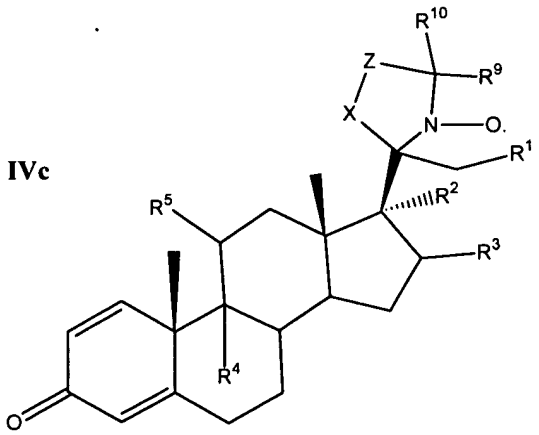
IVa



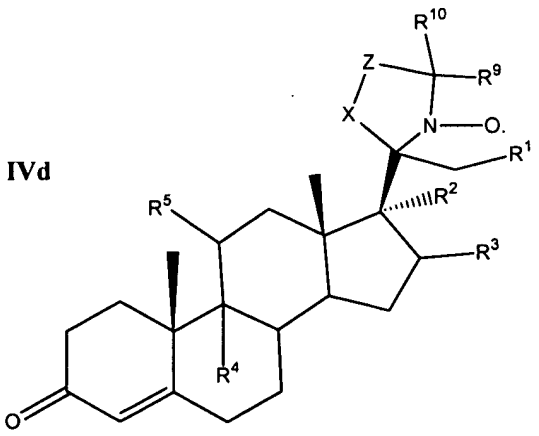
IVb



IVc



IVd



wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^1, R^2, R^5, R^9 or R^{10} comprises at least one NO donor.

Claim 16 (original): Use according to claim 10, wherein said steroid compound has a formula selected from Va to Vd (below) wherein

R^3 is —H, —OH, or —CH_3;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate,

and R^{6A}, if present, is —H , or R^6 and R^{6A} together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C_1-C_5 alkyl groups wherein said alkyl groups may be further substituted by an NO donor, or —$OC(O)R^{12}$, wherein R^{12} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the alkyl group is independently substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

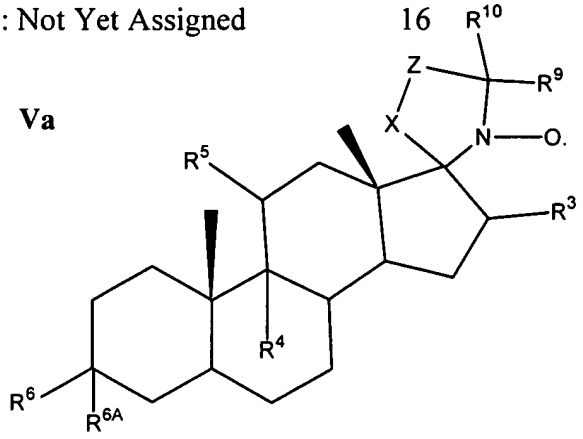
X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

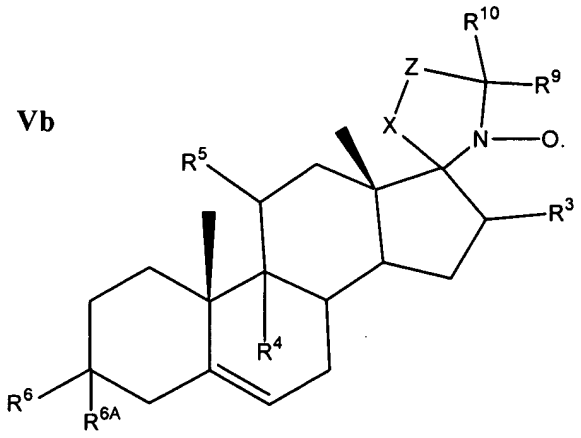
wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^5, R^6, R^9 or R^{10} comprises an NO donor.

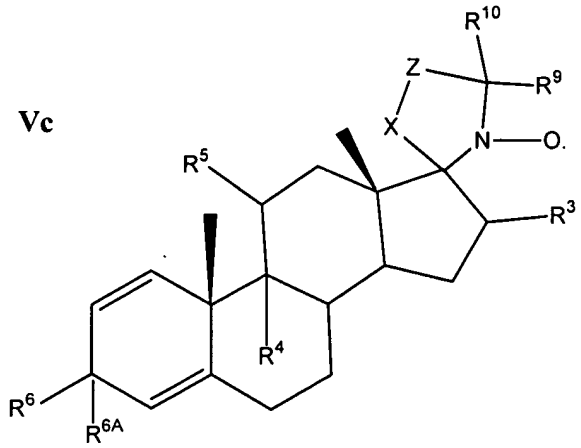
Va


R10
Z
R9
X
N
O.
R5
R3
R4
R6
R6A

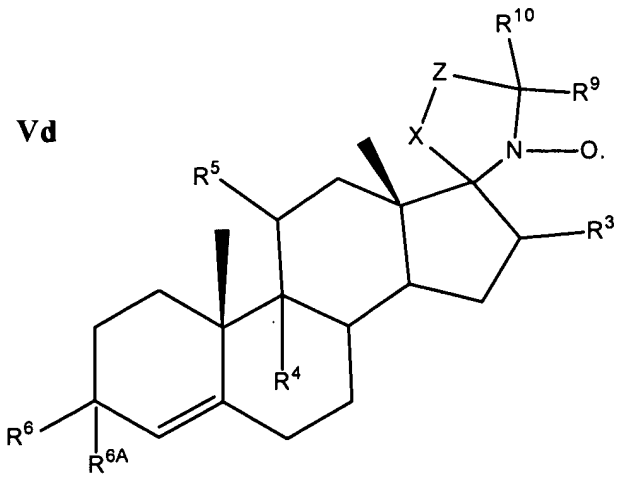
Vb


R10
Z
R9
X
N
O.
R5
R3
R4
R6
R6A

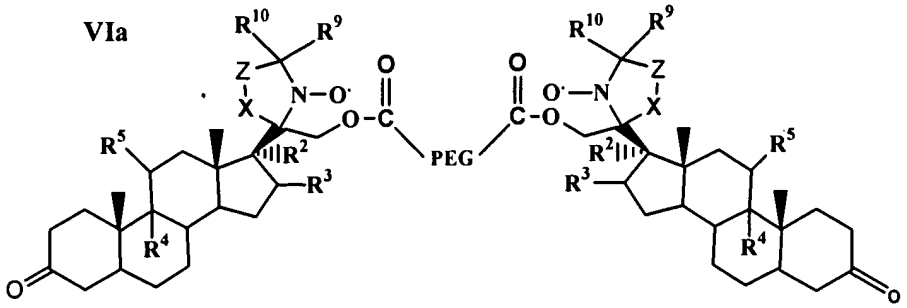
Vc


R10
Z
R9
X
N
O.
R5
R3
R4
R6
R6A

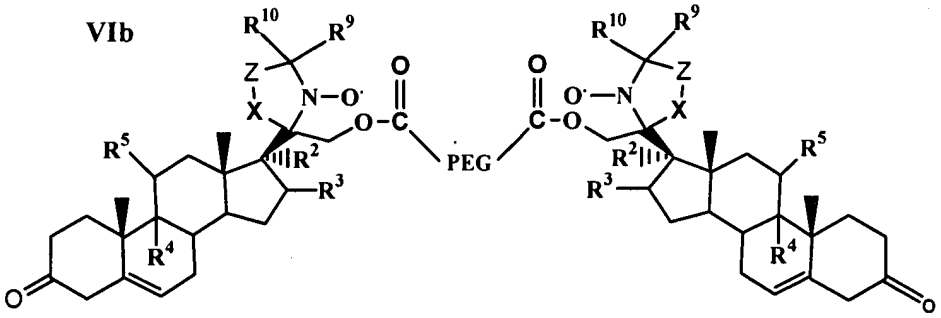
Vd


R10
Z
R9
X
N
O.
R5
R3
R4
R6
R6A

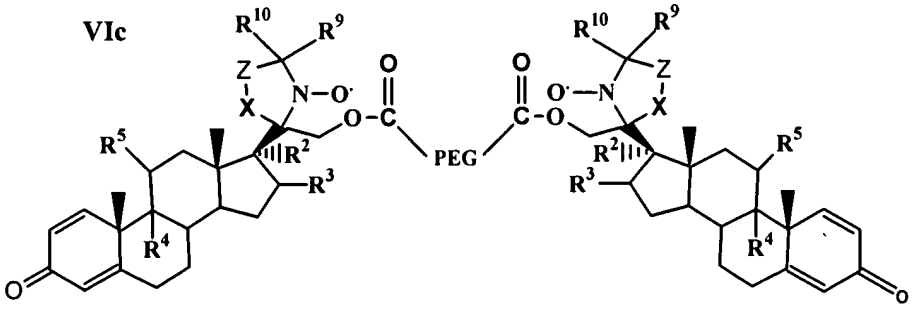
VIa



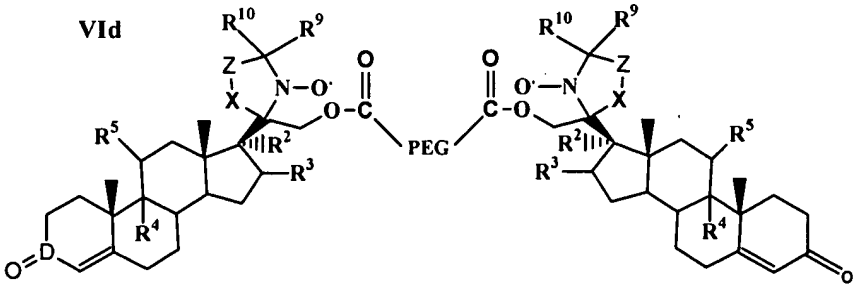
VIb



VIc



VId



Claim 17 (currently amended): Use according to claim 11, wherein said steroid compound has a formula [[a]] selected from VIa to VId (above) wherein

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or

—$OC(O)R^8$, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the alkyl group is independently substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^2, R^5, R^9 or R^{10} comprises at least one NO donor.

Claim 18 (currently amended): Use according to ~~any one of claims 12 to 17~~ claim 10 wherein R^3 is —H, —OH, or —CH_3; R^4 is —H, F, or Cl; and R^5 is —H, =O, or —ONO_2.

Claim 19 (currently amended): Use according to ~~any one of claims 13 to 17~~ claim 11 wherein X is —CH_2— or —O— , Z is —CH_2—, and R^9 and R^{10} are independently methyl or ethyl.

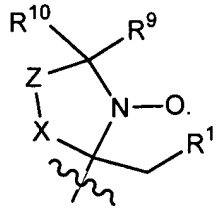
Claim 20 (currently amended): Use according to ~~any one of claims 12 to 15 and 17~~ claim 10 wherein R^2 is —H or —ONO_2.

Claim 21 (currently amended): Use according to ~~any one of claims 12, 14, and 16~~ claim 10 wherein R^6 is =O,—ONO_2, and R^{6A}, if present, is —H , or R^6 and R^{6A} together form a substituted N-oxide

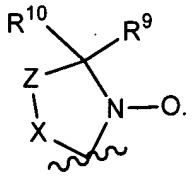
free radical selected from substituted pyrrolidinyloxy N-oxide free radical, substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

Claim 22 (currently amended): Use according to ~~any one of claims 12, 13, and 17~~ claim 10 wherein R^7 is —ONO_2 or a substituted N-oxide free radical selected from substituted pyrrolidinyloxy N-oxide free radical, substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

Claim 23 (currently amended): Use according to ~~any one of claims 12 to 17~~ claim 10 wherein said N-oxide free radical is selected from the substituted 5- or 6- member rings of general formulae 3a and 3b



3a



3b

wherein X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

R^1 is —H, —OH, —$OCOCH_2$-PEG, linear or branched C_1-C_5 alkyl, linear or branched C_1-C_5 alkyl substituted by —ONO, —ONO_2, —SNO, or —NONOate or —$OC(O)R^{15}$, wherein R^{15} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl; and R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups, wherein said alkyl group may be

is independently substituted by —ONO, —ONO_2, —SNO, —NONOate or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl.

Claim 24 (previously presented): A multifunctional steroid compound comprising

i) a steroid component,

ii) at least one SOD mimic component, and

iii) at least one NO donor component,

for use as a medicament.

Claim 25 (original): A multifunctional steroid compound according to claim 24, wherein said steroid component is selected from corticosteroids, estrogens, progesterones, androgens, analogs thereof, and derivatives thereof.

Claim 26 (original): A method of treating or preventing a disorder selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, Chronic Obstructive Pulmonary Diseases (COPDs), bronchial hyperreactivity, respiratory distress syndrome or Chronic Obstructive Airway Disease (COADs), allergic conditions, arthritis, autoimmune hematologic disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-versus-host disease, multiple sclerosis, Alzheimer diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, disorders related to learning, disorders related to olfaction, disorders related to nociception, cerebral edema, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions, drug and disease-induced neuropathies and nephropathies, pathological uterine contractions, sinus tachycardia, ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders,

hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholestemia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion tissue injury, chemotaxis and phagocytic impairment in immunological disorders, aging–mediated changes, cerebrovascular diseases, thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection, in a mammal in need thereof comprising administering to said mammal an effective amount of a a multifunctional steroid compound comprising

i) a steroid component,

ii) at least one SOD mimic component, and optionally

iii) at least one NO donor component.

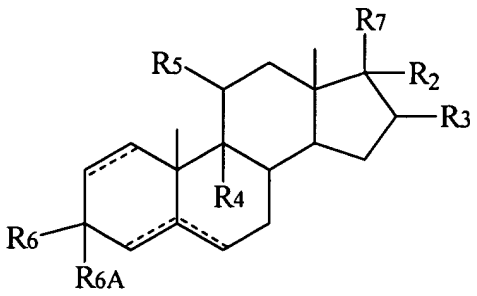
Claim 27 (original): A method according to claim 26, wherein said administration or treatment is selected from the group consisting of topical, oral, and parenteral.

Claim 28 (original): A method according to claim 26, wherein said administration or treatment is selected from the group consisting of suppository, by way of injection, and by way of infusion.

Claim 29 (original): A method according to claim 26, wherein said multifunctional steroid compound is administered by a route selected from intramuscular, intraperitoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, implant, inhalation spray, nasal, vaginal, rectal, sublingual, and urethral.

Claim 30 (original): A method according to claim 26, wherein said mammal is human.

Claim 31 (currently amended): A multifunctional steroid compound of formula (4)



(4)

optical isomers thereof, salts thereof, and solvates thereof;

wherein ----- is a single or double bond, with the proviso that two double bonds are not adjacent;

R^2 is NO donor, —H, —OH, —CH_3, —$OC(O)R^8$ wherein R^8 is C_1-C_5 alkyl or 5- or 6-member heteroaryl, [[or]] or R^2 and R^7 together form a substituted N-oxide free radical;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

R^5 is —H, =O, NO donor or a substituted N-oxide free radical;

R^6 is =O[[,]] or NO donor, and

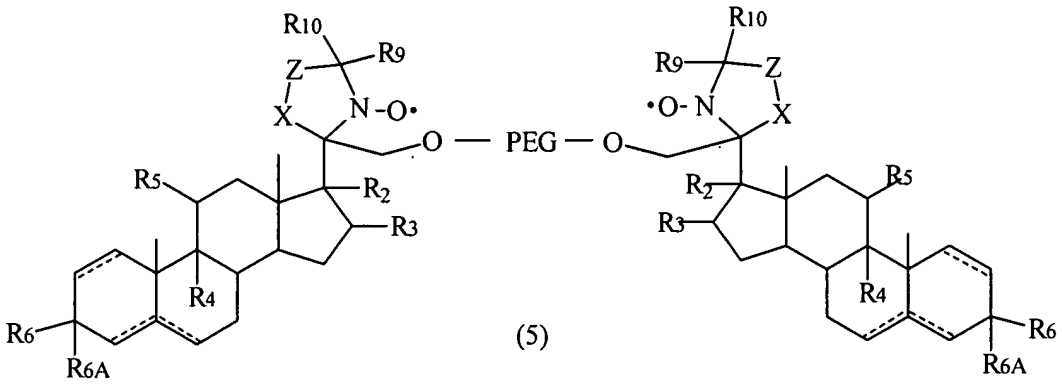
R^{6A}, if present, is —H, or R^6 and R^{6A} together form a substituted N-oxide free radical;

R^7 is —H, NO donor, or a substituted N-oxide free radical wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring, which ring is optionally substituted by —$OCOCH_2$-PEG wherein said PEG may by optionally coupled to another steroid compound, and which ring is further optionally substituted by or one or more independently selected C_1-C_5 alkyl groups which may be further independently substituted by a group selected from an NO donor component, —SR^{11}, —halogen, and —$OC(O)R^{13}$ wherein R^{11} is C_1-C_5 alkyl and wherein R^{13} is C_1-C_5 alkyl or 5- or 6-member heteroaryl, or R^2 and R^7 together form a substituted N-oxide free radical; and

wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups which may be further independently substituted by an NO donor component; and wherein said NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and with the proviso that said compound contains at least one N-oxide free radical and at least one NO donor.

Claim 32 (currently amended): A multifunctional steroid compound according claim 31, wherein said PEG links two identical structures selected from the group consisting of Ia to Id, IIa to IId, [[IIa]] IIIa to IIId, and IVa to IVd.

Claim 33 (original): A compound according to claim 32, having formula (5)



(5)

wherein the R^2, R^3, R^4, R^5, R^6, and R^{6A} are as defined in claim 31;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the alkyl group is independently substituted by an NO donor or —OC(O)R^{14}, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

and PEG is a polyethylene glycol of a molecular weight from about 100 to about 4000.

Claim 34 (original): A compound according to claim 31, having a formula selected from Ia to Id (page 106) wherein

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or —OC(O)R^8, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate, and

R^{6A}, if present, is —H, or R^6 and R^{6A} together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide

free radical is within a 5- or 6- member ring substituted by one or more independently selected C_1-C_5 alkyl groups which may be may be further independently substituted by an NO donor component;

R^7 is —H, —ONO, —ONO_2, —SNO, —NONOate, or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring optionally substituted by —$OCOCH_2$-PEG or one or more independently selected C_1-C_5 alkyl groups which may be further independently substituted by an NO donor component, —SR^{11}— halogen, or —$OC(O)R^{13}$, wherein R^{11} is C_1-C_5 alkyl, and wherein R^{13} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl, or R^2 and R^7 together form a substituted N-oxide free radical; and

NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate;

wherein at least one of R^2, R^5, R^6, or R^7 comprises an NO donor; and

wherein at least one of R^5, R^6, or R^7 comprises a substituted N-oxide free radical.

Claim 35 (original): A compound according to claim 31, having a formula selected from IIa to IId (page 108) wherein

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or

—$OC(O)R^8$, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^7 is —H, —ONO, —ONO_2, —SNO, —NONOate, or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by

—$OCOCH_2$-PEG or by one or more independently selected C_1-C_5 alkyl groups, wherein said alkyl group may be further independently substituted by an NO donor, —SR^{11}, —halogen, or —$OC(O)R^{13}$, wherein R^{11} is C_1-C_5 alkyl, and wherein R^{13} is C_1-C_5 alkyl or 5- or 6-member heteroaryl;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups or substituted linear or branched C_1-C_5 alkyl groups wherein said alkyl group may be substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl or 5- or 6-member heteroaryl;

X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^2, R^5, R^7, R^9 or R^{10} comprises an NO donor.

Claim 36 (original): A compound according to claim 31, having a formula selected from IIIa to IIId (page 110) wherein

R^1 is —H, —OH, —$OCOCH_2$-PEG, linear or branched C_1-C_5 alkyl, linear or branched C_1-C_2 alkyl substituted by an NO donor,—SR^{11}, —halogen, or —$OC(O)R^{15}$, wherein R^{11} is C_1-C_5 alkyl, wherein R^{15} is C_1-C_5 alkyl;

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or

—$OC(O)R^8$, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate, and R^{6A} if present is —H, or R^6 and R^{6A} together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more

independently selected C_1-C_5 alkyl groups, wherein said alkyl may be further substituted by an NO donor, or —OC(O)R^{12}, wherein R^{12} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;
R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein said alkyl group is independently substituted by —ONO, —ONO_2, —SNO, —NONOate or —OC(O)R^{14}, wherein R^{14} is C_1-C_5 alkyl;
X is —CH_2—, —O— or —S—;
Z is —CH_2— or —CH_2-CH_2—;
wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and
wherein at least one of R^1, R^2, R^5, R^6, R^9 or R^{10} comprises at least one NO donor.

Claim 37 (original): A compound according to claim 31, having a formula selected from IVa to IVd (page 112) wherein
R^1 is —H, —OH, —OCOCH_2-PEG; linear or branched C_1-C_5 alkyl; linear or branched C_1-C_5 alkyl substituted by an NO donor, —SR^{11}, —halogen, or —OC(O)R^{15}, wherein R^{11} is C_1-C_5 alkyl, and wherein R^{15} is C_1-C_5 alkyl;
R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or
—OC(O)R^8, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;
R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;
R^4 is —H or halogen;
R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups; R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the said group is independently substituted by an NO donor or —OC(O)R^{14}, wherein R^{14} is C_1-C_5 alkyl;
X is —CH_2—, —O— or —S—;
Z is —CH_2— or —CH_2-CH_2—;

wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^1, R^2, R^5, R^9 or R^{10} comprises at least one NO donor.

Claim 38 (original): A compound according to claim 31, having a formula selected from Va to Vd (page 114) wherein

R^3 is —H, —OH, or —CH_3;

R^4 is —H or halogen;

R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;

R^6 is =O, —ONO, —ONO_2, —SNO, —NONOate,

and R^{6A}, if present, is —H , or R^6 and R^{6A} together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C_1-C_5 alkyl groups wherein said alkyl groups may be further substituted by an NO donor, or —$OC(O)R^{12}$, wherein R^{12} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the alkyl group is independently substituted by an NO donor or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;

X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and

wherein at least one of R^5, R^6, R^9 or R^{10} comprises an NO donor.

Claim 39 (original): A compound according to claim 32, having a formula selected from VIa to VId (page 115) wherein

R^2 is —H, —ONO, —ONO_2, —SNO, —OH, —CH_3, —NONOate, or —OC(O)R^8, wherein R^8 is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;
R^3 is —H, —OH, or —CH_3, or R^2 and R^3 together form a heterocyclic ring;
R^4 is —H or halogen;
R^5 is —H, =O, —ONO, —ONO_2, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6-member ring substituted by one or more independently selected C_1-C_5 alkyl groups;
R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups wherein the alkyl group is independently substituted by an NO donor or —OC(O)R^{14}, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl;
X is —CH_2—, —O— or —S—;
Z is —CH_2— or —CH_2-CH_2—;
wherein an NO donor is a group comprising one of —ONO_2, —ONO, —SNO, and —NONOate; and
wherein at least one of R^2, R^5, R^9 or R^{10} comprises at least one NO donor.

Claim 40 (currently amended): A compound according to ~~any one of claims 34 to 39~~ claim 31 wherein R^3 is —H, —OH, or —CH_3; R^4 is —H, F, or Cl; and R^5 is —H, =O, or —ONO_2.

Claim 41 (currently amended): A compound according to ~~any one of claims 35 to 39~~ claim 33 wherein X is —CH_2— or —O— , Z is —CH_2—, and R^9 and R^{10} are independently methyl or ethyl.

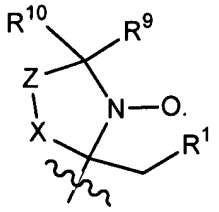
Claim 42 (currently amended): A compound according to ~~any one of claims 34-37 and 39~~ claim 31 wherein R^2 is —H or —ONO_2.

Claim 43 (currently amended): A compound according to ~~any one of claims 34, 36 and 38~~ claim 31 wherein R^6 is =O,—ONO_2, and R^{6A}, if present, is —H , or R^6 and R^{6A} together form a substituted N-oxide free radical selected from substituted pyrrolidinyloxy N-oxide free radical, substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted

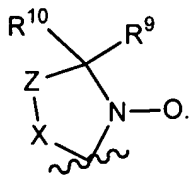
oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

Claim 44 (currently amended): A compound according to ~~any one of claims 34, 35 and 39~~ claim 31 wherein R^7 is —ONO_2 or a substituted N-oxide free radical selected from substituted pyrrolidinyloxy N-oxide free radical, substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

Claim 45 (currently amended): A compound according to ~~any one of claims 34 to 39~~ claim 31 wherein said N-oxide free radical is selected from the substituted 5- or 6- member rings of general formulae 3a and 3b



3a



3b

wherein X is —CH_2—, —O— or —S—;

Z is —CH_2— or —CH_2-CH_2—;

R^1 is —H, —OH, —$OCOCH_2$-PEG, linear or branched C_1-C_5 alkyl, linear or branched C_1-C_5 alkyl substituted by —ONO, —ONO_2, —SNO, or —NONOate or —$OC(O)R^{15}$, wherein R^{15} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl; and R^9 and R^{10} are independently, linear or branched C_1-C_5 alkyl groups, or substituted linear or branched C_1-C_5 alkyl groups, wherein said alkyl group may be

is independently substituted by —ONO, —ONO_2, —SNO, —NONOate or —$OC(O)R^{14}$, wherein R^{14} is C_1-C_5 alkyl, or 5- or 6-member heteroaryl.

Claim 46 (currently amended): A pharmaceutical composition comprising a compound according to ~~any one of claims 31 to 45~~ claim 31.

Claim 47 (original): A pharmaceutical composition according to claim 46, further comprising a component selected from carrier, binding agent, stabilizer, adjuvant, diluent, excipient, surfactant, odorant, and second pharmaceutically active agent.

Claim 48 (currently amended): A pharmaceutical composition according to ~~claims 46 or 47,~~ claim 46, for use as a medicament in treating and preventing a disorder selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, pneumonia, Chronic Obstructive Pulmonary Diseases (COPDs), bronchial hyperreactivity, respiratory distress syndrome or Chronic Obstructive Airway Disease (COADs), allergic conditions, arthritis, autoimmune hematologic disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-versus-host disease, multiple sclerosis, Alzheimer diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, disorders related to learning, disorders related to olfaction, disorders related to nociception, cerebral edema, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions, drug and disease-induced neuropathies and nephropathies, pathological uterine contractions, sinus tachycardia, ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders, hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholestemia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes

mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion tissue injury, chemotaxis and phagocytic impairment in immunological disorders, aging–mediated changes, cerebrovascular diseases, thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection.

Claim 49 (original): A kit for administration of a multifunctional steroid compound comprising i) a dosage amount of at least one multifunctional steroid compound that comprises a steroid component, at least one SOD mimic component, and optionally at least one NO donor component;

ii) instructions for use; and

iii) optionally means for the delivery of said compound.

Claim 50 (original): A kit according to claim 49 comprising one of items selected from inhaler, spray dispenser, syringe, or suppositories.